Department of Veterans Affairs **VHA DIRECTIVE 2000-038**
Veterans Health Administration
Washington, DC 20420 **October 12, 2000**

INFLUENZA VACCINE – RECOMMENDATIONS FOR 2000-2001

1. PURPOSE: This Veterans Health Administration (VHA) Directive provides guidance on the use of the influenza vaccine for 2000-2001.

2. BACKGROUND

a. For several years the Department of Veterans Affairs (VA) has provided influenza vaccine to high-risk patients and to employees. Information is provided on vaccine composition, usage (including high-risk groups), contraindications, side effects and adverse reactions, dosage, and related preventive strategies (see Attachment A). The program will continue to receive increased emphasis as a part of the VA Preventive Medicine Program and will be assessed based on doses dispensed.

b. The trivalent influenza vaccine prepared for the 2000-2001 season will include A/Moscow/10/99 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Beijing/184/93-like antigens. For the A/Moscow/10/99 (H3N2)-like antigen, U.S. manufacturers will use the antigenically equivalent A/Panama/2007/99 (H3N2) virus and for the B/Beijing/184/93-like antigen, they will use the antigenically equivalent B/Yamanashi/166/98 virus; these viruses will be used because of their growth properties and because they are representative of currently circulating A (H3N2) and B viruses.

3. POLICY: It is the VHA policy to publish annual recommendations on the use of the influenza vaccine.

4. ACTION

a. VHA Headquarters recommends that the immunization program outlined by the Advisory Committee on Immunization Practices and published in Morbidity and Mortality Weekly Report (MMWR), April 14, 2000:Vol. 49: No. RR-3; 1-38 be followed by VA health care facilities.

b. VA Form 10-5549, Influenza Vaccine Consent Form, (see Att. B) is to be completed by all employees receiving influenza vaccine. ***NOTE:*** *These forms are to be locally reproduced.* The forms may be used for patients as a local option, but written informed consent is not required when the vaccine is administered in the context of a regular "practitioner-patient" relationship.

c. If an influenza vaccine delay and/or shortage should occur, VHA facilities at the local level must develop a prioritization plan that will maximize protection of patients most likely to develop serious and life-threatening complications from influenza.

THIS VHA DIRECTIVE EXPIRES OCTOBER 31, 2001

5. REFERENCES

a. Centers for Disease Control and Prevention (CDC). "Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP)," MMWR. Vol. 49 (No. RR-3); pp. 1-38: April 14, 2000.

b. CDC. "Neuraminidase Inhibitors for Treatment of Influenza A and B Infections," MMWR. Vol. 48 (No. RR-14): December 17, 1999.

c. CDC. "Notice to Readers: Delayed Supply of Influenza Vaccine and Adjunct ACIP Influenza Vaccine Recommendations for the 2000-01 Influenza Season," MMWR. Vol. 49(27): pp. 619-622: July 14, 2000.

d. Physicians' Desk Reference, 54th Edition. Ronald Arky, Medical Consultant, Medical Economics Co., Inc. Product Information Wyeth-Ayerst Laboratories, pp. 3256-3257: 2000.

e. CDC. "Notice to Readers: Updated Recommendations from the Advisory Committee on Immunization Practices in Response to Delays in Supply of Influenza Vaccine for the 2000-01 Season. MMWR, October 6, 2000 / Vol. 49 (39); 888-892.

6. FOLLOW-UP RESPONSIBILITY: The Chief, Patient Care Services Officer, (11) is responsible for the contents of this Directive. Questions relating to the clinical aspects of the influenza immunization program may be referred to the Office of the Program Director for Infectious Diseases, Gary A. Roselle, M.D., at (513) 475-6398

7. RECISSION: VHA Directive 99-046 is rescinded. This Directive will expire on October 31, 2001.

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Under Secretary for Health

Attachment

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ATTACHMENT A

INFORMATION ABOUT THE INFLUENZA VIRUS VACCINE FOR 2000 - 2001

1. Target Groups for Vaccination

a. **High-risk Groups.** Vaccination is recommended for the following groups of persons who are at increased risk for complications from influenza or who have a higher prevalence of chronic medical conditions that place them at risk for influenza-related complications:

(1) Persons aged ≥50 years;

(2) Residents of nursing homes, other chronic-care facilities that house persons of any age who have chronic medical conditions, and residents of domiciliaries;

(3) Adults who have chronic disorders of the pulmonary or cardiovascular systems, including asthma;

(4) Adults who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobulinopathies, or immunosuppression (including immunosuppression caused by medications or by human immunodeficiency virus); and

(5) Women who will be in the second or third trimester of pregnancy during the influenza season.

b. **Persons Who Can Transmit Influenza to Those at High Risk**

(1) Physicians, nurses, and other personnel in both hospital and outpatient-care settings, including emergency response workers;

(2) Employees of nursing homes and chronic-care facilities who have contact with patients or residents;

(3) Employees of assisted living and other residences for persons in high-risk groups;

(4) Providers of home care (e.g., visiting nurses and volunteer workers) to persons in high-risk groups; and

(5) Household members of persons in high-risk groups.

c. **Vaccination of Other Groups**

(1) Pregnant Women. Influenza-associated excess deaths among pregnant women were documented during the pandemics of 1918-1919 and 1957-1958. Case reports and limited studies also suggest that pregnancy can increase the risk for serious medical complications of influenza as a result of increases in heart rate, stroke volume, and oxygen consumption; decreases in lung capacity; and changes in immunologic function. Women who will be beyond the first

trimester of pregnancy (greater than or equal to 14 weeks' gestation) during the influenza season should be vaccinated. Pregnant women who have medical conditions that increase their risk for complications from influenza should be vaccinated before the influenza season, regardless of the stage of pregnancy. Because currently available influenza vaccine is an inactivated vaccine, many experts consider influenza vaccination safe during any stage of pregnancy. Some experts prefer to administer influenza vaccine during the second trimester to avoid a coincidental association with spontaneous abortion, which is common in the first trimester, and because exposures to vaccines traditionally have been avoided during the first trimester.

(2) Breastfeeding Mothers. Influenza vaccine does not affect the safety of mothers who are breastfeeding or their infants. Breastfeeding does not adversely affect the immune response and is not a contraindication for vaccination.

(3) Travelers

(a) The risk of exposure to influenza during travel depends on the time of year and destination. In the tropics, influenza can occur throughout the year. In the temperate regions of the southern hemisphere, most influenza activity occurs from April through September. In temperate climate zones of the northern and southern hemispheres, travelers also can be exposed to influenza during the summer, especially when traveling as part of large organized tourist groups that include persons from areas of the world where influenza viruses are circulating.

(b) Persons at high risk for complications for influenza who were not vaccinated with influenza vaccine during the preceding fall or winter should consider receiving influenza vaccine before travel if they plan to a) travel to the tropics; b) travel with large organized tourist groups at any time of year, or c) travel to the southern hemisphere from April through September. No information is available regarding the benefits of revaccinating persons before summer travel who were already vaccinated in the preceding fall. Persons at high risk who received the previous season's vaccine before travel should be revaccinated with the current vaccine in the following fall or winter. Persons aged $\geq$ 50 years and others at high risk might wish to consult with their physicians before embarking on travel during the summer to discuss the symptoms and risks of influenza and the advisability of carrying antiviral medications for either prophylaxis or treatment of influenza.

(4) General Population. Physicians should administer influenza vaccine to any person who wishes to reduce the likelihood of becoming ill with influenza. Persons who provide essential community services should be considered for vaccination to minimize disruption of essential activities during influenza outbreaks. Students or other persons in institutional settings (e.g., those who reside in dormitories) should be encouraged to receive vaccine to minimize the disruption of routine activities during epidemics.

3. Persons Who Should Not be Vaccinated

a. Inactivated influenza vaccine should not be administered to persons known to have anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine without first consulting a physician (see 3. Side Effects and Adverse Reactions). Prophylactic use of the antiviral agents amantadine or rimantadine is an option for preventing influenza A among such persons. However, persons who have a history of anaphylactic hypersensitivity to vaccine components but who are also at high risk for complications of influenza can benefit from vaccine after appropriate allergy evaluation and desensitization. Information about vaccine components can be found in package inserts from each manufacturer.

b. Persons with acute febrile illness usually should not be vaccinated until their symptoms have abated. However, minor illnesses with or without fever do not contraindicate the use of influenza vaccine, particularly among children with mild upper respiratory tract infection or allergic rhinitis.

4. Side Effects and Adverse Reactions

a. Inactivated influenza vaccine contains noninfectious killed viruses and cannot cause influenza. Coincidental respiratory disease unrelated to influenza vaccination can occur after vaccination. The most frequent side effect of vaccination is soreness at the vaccination site that lasts up to 2 days. These local reactions generally are mild and rarely interfere with the person's ability to conduct usual daily activities. Systemic reactions include the following:

(1) Fever, malaise, myalgia, and other systemic symptoms can occur following vaccination and most often affect persons who have had no exposure to the influenza virus antigens in the vaccine (e.g., young children). These reactions begin 6 to 12 hours after vaccination and can persist for 1 to 2 days.

(2) Immediate, presumably allergic, reactions (e.g., hives, angioedema, allergic asthma, and systemic anaphylaxis) rarely occur after influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component; most reactions likely are caused by residual egg protein. Although current influenza vaccines contain only a small quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Persons who have developed hives, have had swelling of the lips or tongue or have experienced acute respiratory distress or collapse after eating eggs should consult a physician for appropriate evaluation to help determine if vaccine should be administered. Persons with documented immunoglobulin E (IgE)-mediated hypersensitivity to eggs, including those who have had occupational asthma or other allergic responses to egg protein, might also be at increased risk for allergic reactions to influenza vaccine, and consultation with a physician should be considered.

(a) Hypersensitivity reactions to any vaccine component can occur. Although exposure to vaccines containing thimerosal can lead to induction of hypersensitivity, most patients do not develop reactions to thimerosal when administered as a component of vaccines, even when patch or intradermal tests for thimerosal indicate hypersensitivity. When reported, hypersensitivity to thimerosal usually has consisted of local, delayed-type hypersensitivity reactions.

(b) Although the 1976 swine influenza vaccine was associated with an increased frequency of Guillain-Barre′ syndrome (GBS), evidence for a casual relationship of GBS with subsequent vaccines prepared from other virus strains is less clear. Obtaining strong epidemiologic evidence for a possible small increase in risk is difficult for a rare condition such as GBS, which has an annual incidence of only 10 to 20 cases per million adults. During three of four influenza seasons studied from 1977 through 1991, the overall relative risk estimates for GBS after influenza vaccination were slightly elevated but were not statistically significant in any of these studies. However, in a study of the 1992-93 and 1993-94 seasons, the overall relative risk for GBS was 1.7 (95 percent confidence interval = 1.0-2.8; p=0.04) during the 6 weeks following vaccination, representing an excess of slightly more than one additional case of GBS per million persons vaccinated; the combined number of GBS cases peaked 2 weeks after vaccination. Thus, investigations to date suggest no large increase in GBS associated with influenza vaccines (other than the swine influenza vaccine in 1976) and that if influenza vaccine does pose a risk, it is probably quite small, slightly more than one additional case per million persons vaccinated. Even if GBS were a true side effect of vaccination in the years after 1976, the estimated risk for GBS of slightly more than one additional case per million persons vaccinated is substantially less than the risk for severe influenza, which could be prevented by vaccination, all age groups, especially persons aged $\geq$65 years and those who have medical indications for influenza vaccination. The potential benefits of influenza vaccination in preventing serious illness, hospitalization, and death greatly outweigh the possible risks for developing vaccine-associated GBS. The average case-fatality ratio for GBS is 6 percent and increases with age. However, no evidence indicates that the case-fatality ratio for GBS differs among vaccinated persons and those not vaccinated. Whereas the incidence of GBS in the general population is very low, persons with a history of GBS have a substantially greater likelihood of subsequently developing GBS than persons without such a history. Thus, the likelihood of coincidentally developing GBS after influenza vaccination is expected to be greater among persons with a history of GBS than among persons with no history of this syndrome. Whether influenza vaccination specifically might increase the risk for recurrence of GBS is not known. Therefore, it would seem prudent to avoid influenza vaccination of persons who are not at high risk for severe influenza complications and who are known to have developed GBS within 6 weeks of a previous influenza vaccination. However, many experts believe that for most persons who have a history of GBS and who are at high risk for severe complications from influenza, the established benefits of influenza vaccination justify yearly vaccination.

(c) Hypoprothombinemia. In patients receiving warfarin and elevated theophylline serum concentrations have occurred. Most studies have failed to show any adverse effects of influenza vaccine in patients receiving these drugs. Nevertheless, monitoring for possible enhanced drug effect or toxicity is indicated for those persons taking theophylline preparations or warfarin sodium.

4. Vaccine Dosage. Adult patients (>12 yrs.) should receive one intramuscular dose in the deltoid muscle of 0.50 mL of whole or split-virus containing 15 μg each of A/Moscow/10/99 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Beijing 184/93-like antigens.

5. Timing for Annual Vaccination. The optimal time to vaccinate persons in high-risk groups is usually from the beginning of October through mid-November, because influenza activity in

the United States generally peaks between late December and early March. Administering vaccine before October should generally be avoided in facilities such as nursing homes, because antibody levels can begin to decline within a few months after vaccination. To avoid missed opportunities for vaccination, beginning each September, influenza vaccine should be offered to persons at high risk when they are seen by health care providers for routine care or are hospitalized, provided that vaccine is available. If regional influenza activity is expected to begin earlier than December, vaccination programs also can be undertaken as early as September. Health care providers should offer vaccine to unvaccinated persons even after influenza virus activity is documented in a community and should continue to offer vaccine throughout the influenza season.

6. Simultaneous Administration of Other Vaccines. The target groups for influenza and pneumococcal vaccination overlap considerably. For persons at high risk who to have not previously been vaccinated with pneumococcal vaccine, health care providers should strongly consider administering pneumococcal and influenza vaccines concurrently. Both vaccines can be administered at the same time at different sites without increasing side effects. However, influenza vaccine is administered each year, whereas pneumococcal vaccine is not.

7. Antiviral Agents for Influenza. Antiviral drugs for influenza are an important adjunct to influenza vaccine for the ocntrol and prevention of influenza. However, they are not a substitute for vaccination. Four currently licensed agents are available in the United States: amantadine, rimantadine, zanamivir, and oseltamivir. Amantadine and rimantadine are chemically related antiviral drugs with activity against influenza A viruses, but not influenza B viruses. Amantadine was approved in 1966 for prophylaxis of influenza A (H2N2) infection and was later approved in 1976 for the treatment and prophylaxis of influenza type A virus infections in adults and children aged $\geq$1 year. Rimantadine was approved in 1993 for treatment and prophylaxis of infection in adults. Zanamivir and oseltamivir are neuraminidase inhibitors with activity against both influenza A and B viruses. Both zanamivir and oseltamivir were approved in 1999 for the treatment of uncomplicated influenza infections, but neither have yet been approved for prophylaxis. Zanamivir was approved for treatment for persons aged $\geq$12 years, and oseltamivir was approved for treatment for persons aged $\geq$18 years. The four drugs differ in terms of their pharmacokinetics, side effects, and costs. Consult the package inserts for more information.

8. Department of veterans Affairs (VA) Medical Center Employees. In recent years many VA medical centers have offered the vaccine (free of charge) because employees may transmit influenza to patients. Influenza vaccine should be offered to employees through the Employee Health Unit for the purpose of protecting patients served by VA. Immunization records will be maintained in the Employee Health Unit. Expenses involved in this program should be kept at a minimum, and for this reason, the use of centrally-procured vaccine vials is recommended instead of unit dose vaccine.

ATTACHMENT B

VA FORM 10-5549, INFLUENZA VACCINE CONSENT FORM

1. The Disease. Influenza (flu) is caused by viruses. When people get flu they may have fever, chills, headache, dry cough or muscle aches. Illness may last several days or a week or more, and complete recovery is usual. However, complications may lead to pneumonia or death in some people. For the elderly and people with diabetes or heart, lung, or kidney diseases, flu may be especially serious.

2. The Vaccine. Today's flu vaccines cause fewer side effects than those used in the past. In contrast with some other vaccines, flu vaccine can be taken safely during pregnancy; however, flu vaccine should be given to pregnant women according to the chronic illness criteria applied to other persons. One shot will protect most people from influenza during the next flu season.

3. Possible Vaccine Side Effects. Most people will have no side effects from the vaccine. However, tenderness at the site of the shot may occur and last for several days. Some people will also have fever, chills, headache, or muscle aches within the first 48 hours.

4. Special Precautions. As with any vaccine or drug, the possibility of severe or potentially fatal reactions exists. However, flu vaccine has rarely been associated with severe or fatal reactions. An uncommon illness characterized by ascending paralysis (Guillain-Barre′ Syndrome) has been reported following other flu vaccines, but not in association with this flu vaccine; however, it must be assumed that the risk is present. Hypersensitivity reactions to any vaccine component can occur. Exposure to vaccines containing thimerosal can lead to induction of hypersensitivity. When reported, hypersensitivity to thimerosal has usually consisted of local, delayed-type hypersensitivity reactions (localized swelling and redness). In some instances people receiving vaccine have had allergic reactions. The following precautions should be carefully noted:

a. People with known allergy to eggs should receive the vaccine only for specific indications and under special medical supervision.
b. People with fever should delay getting vaccinated until the fever is gone.
c. People who have received another type of vaccine in the past 14 days should consult a physician before taking the flu vaccine.

NOTE: *Please ask if you have any questions about the flu or the flu vaccine.*

CONSENT FORM

I have read the above statement about influenza (flu), the vaccine, and the special precautions. I have had an opportunity to ask questions, and understand the benefits and risks of flu vaccination. I request that it be given to me, or to the person named below of whom I am the parent or guardian.

_____ _____
Name of Person to Receive Vaccine (Please Print) Date Vaccinated

_____ _____
Signature of Person Receiving Vaccine or Parent or Guardian Manufacturer and Lot No.

_____
Date Signed

VA Form 10-5549
Aug 1998